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Candidiasis in the Burned Patient

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Candida **organisms were cultured from 452 of 1,513 hospitalized burned patients during a 6-year study period. Of the 172 patients with colonization of the eschar by this fungus, only 20.7% subsequently developed invasive candidal sepsis. The mortality of untreated *Candida* burn wound infection was 100%, and with aggressive medical-surgical therapy, 91.6%. Candidemia was present in 52 patients and 76.9% of these died.**

Candida **infection was seen as a preterminal phenomenon, coincident with a generalized collapse of patients' defensive and homeostatic mechanisms. For this reason, mortality was high and the infection rarely responded to treatment.**

Control of this lethal complication rests with prevention by the judicious use of intravenous broad-spectrum antibiotics and expeditious closure of the burn wound.

Infectious complications are the most common cause of death in burned patients following the resuscitation phase. Topical and intravenous antibiotics employed to treat or suppress bacterial infection allow the emergence of resistant microbes such as fungi, particularly *Candida sp.* As a colonial organism of the eschar or mucosal surfaces, *Candida* is a harmless saprophyte, but as an invader of the blood stream or burn wound, it is a dangerous pathogen. The spectrum of disease caused by this organism in thermally injured patients was reviewed and current treatment modalities evaluated.

MATERIALS AND METHODS

Records of patients hospitalized at the U.S. Army Institute of Surgical Research Burn Unit during 1973 through 1978 were evaluated and all those from whom *Candida sp.* was cultured at any time during their hospital course were selected for study. All patients received wound care that was generally uniform, consisting of alternating topical applications of mafenide acetate (Sulfamylon, Winthrop, New York, NY) and silver sulfadiazine (Silvadene, Marion, Kansas City, MO) every 12 hours. Polyethylene intravenous catheters were changed 48 to 72 hours after placement and silastic urinary bladder catheters and tracheostomy tubes were changed weekly.

All patients were routinely monitored with swab burn wound cultures (6), and cultures of samples of blood, urine, and sputum three times weekly. More frequent cultures were obtained as indicated by each patient's clinical course.

Nystatin was routinely administered orally to all patients during the first 2 years of the study, intermittently in the next 3 years and not at all in the final year of study. No prophylactic systemic antibiotics were employed. Intravenous antibiotics were administered according to the laboratory sensitivity of the bacteria cultured but frequently consisted of vancomycin and amikacin. Amphotericin B was administered only when clinical signs of candidal sepsis were evident and two or more blood cultures positive for the organism were obtained.

Invasion of the burn wound by *Candida* was defined as the penetration of the organism into viable tissue as evidenced by a simultaneous wound and blood culture of the fungus or microscopic demonstration of pseudohyphae within viable tissue. Those with concomitant mycotic invasion by other genera of fungi were eliminated from consideration.

RESULTS

During this 6-year period 1,513 burned patients were admitted and treated. Of these 521 (34.4%) had fungi cultured from them during their hospitalization. *Candida* species were recovered from 452 (86.7%) of the 521. Only 20.7% of patients with colonization of the eschar subsequently developed *Candida* burn wound invasion. Table I summarizes the culture data.

Thirty-six patients developed *Candida* burn wound invasion. Table II summarizes their characteristics in relation to the burned population as a whole, and therapeutic modalities used in the treatment of established

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burn wound invasion are summarized in Table III. Two of the three survivors were managed with aggressive surgical debridement of the infected wound. One of these also received adjuvant amphotericin B. The third survivor received only amphotericin B and a conservative approach to the management of this burn wound was undertaken.

Of patients with *Candida* burn wound infection 75% also had candidemia. Considering all sources, a total of 52 patients had positive blood cultures for *Candida;* in 27 of those the burn wound was the septic focus. Fifteen patients manifested candidemia and burn wound invasion by other noncandidal fungal organisms. Candidemia was present in ten patients with no apparent site of origin (Table I). The characteristics of this subgroup are summarized in Table II.

Of all patients with candidemia 76.9% died. Fourteen of the 52 patients with positive blood cultures received amphotericin B and the mortality in this subgroup was 92.8%.

TABLE I
Culture data

Source of *Candida* Organisms	Number of Patients	
	Total Isolates*	Only Source
Burn wound	172	98
Urine	130	55
Postmortem tissue	117	75
Sputum	89	26
Blood	52	10
Other	41	14
'Thrush'	7	2

* This column reflects multiple sources from a single patient.

TABLE II
Patient populations

	General Population	*Candida* Burn Wound Invasion	Candidemia without Wound Invasion
Numbers of patients	1,513	36	10
Age (yrs)	29.3	37.0	33.4
Percentage of total body surface injured	38.6%	56.1%	46.5%
Percentage full-thickness injury	16.5%	35.7%	33.6%
Mortality (%)	34.2%	91.6%	60.0%

TABLE III
Forms of therapy for *Candida* burn wound invasion

Treatments	Totals	Survivors
None	15	None
Surgical debridement	12	2
Amphotericin B alone	7	1
Adjuvant	4	1
Amputation	2	None

DISCUSSION

Thermally injured patients are a population at risk for *Candida* sepsis (10, 15, 17). Multiple systems are directly or indirectly injured or stressed to the limits of their reserves. Nutritional deficits may arise as their clinical course progresses for which intravenous alimentation may be required (16). Bacterial sepsis, topical antimicrobial agents, and systemic antibiotics, as well as chronic indwelling cannulae, create favorable circumstances for the colonization and subsequent invasion by this fungus (6–8).

Colonization always preceded invasive sepsis, but 80% of patients colonized lived in an equilibrium in which the presence of the fungus did not alter their clinical course. This delicate balance was usually upset by an episode of bacterial sepsis, hemorrhage, or hypotension that further stressed and compromised the patients. This permitted the colonizing organisms to invade and proliferate within viable tissue.

Invasive infection by this organism is rare (9, 10). Although *Candida sp.* was by far the most common nonbacterial organism cultured in this review (86.7%), it caused only one third of the 107 mycotic infections seen during the study. Eleven per cent of all burned patients became colonized by *Candida sp.*, but only 3.4% developed septicemia and only 2.4% developed candidal burn wound invasion.

Candida invasion of the burn wound is a dangerous complication, the mortality of which approaches 100%. Therapeutic modalities currently available did not significantly alter the course of the infection (Table III).

One week is required to identify *Candida* in blood cultures. Its presence was frequently considered a contaminant until a second or third culture confirmed its presence (3). The institution of intravenous amphotericin B after this considerable delay was too frequently a futile gesture (3, 5, 13).

Table II demonstrates that those patients with *Candida* burn wound infections are older and more extensively injured than the general burned patient population or those with candidemia alone. Mortality of thermally injured patients generally increases with both age and magnitude of injury. The high mortality of the infection in this review, compared to other published series in nonburn populations, suggests that *Candida* invasion was often a result rather than a cause of a generalized collapse of host defense and homeostatic mechanisms (8, 11, 12).

Urine cultures were second in frequency to the burn wound as a source of *Candida* isolates, but rarely the source of invasive sepsis. The need to maintain bladder intubation on a long-term basis, even in the presence of the organism in urine culture, perpetuated the presence of the fungus in the urinary tract (8). Despite this, only one patient suffered *Candida* sepsis by way of the urinary

tract from a renal abscess (7). The exophytic lesions of the bladder resulting from long-term catheterization were frequently interlaced with pseudohyphae, but the bladder wall itself was never invaded. This also negated in the burn patient the frequently cited 'usefulness' of urine cultures as an indicator of distant *Candida* infection (6).

Equally well described is the frequency that the gastrointestinal tract is the source of *Candida* sepsis in nonburned, immunosuppressed patients (4, 17). However, in the present study, only one patient demonstrated evidence of candidal proliferation in and invasion of the gastrointestinal tract. Only two of the seven patients with oropharyngeal candidiasis (thrush) subsequently manifested *Candida* septicemia. None of these subsequently developed gastrointestinal tract invasion. This patient population differs markedly from those in which this infectious complication has been previously described. In this series, the burn wound was by far the major focus of proliferation of *Candida sp.* and candidal infection.

Management of this dangerous, infectious complication rests with prevention. Aggressive surgical management and expeditious closure of the burn wound before the onset of invasive sepsis, and restriction of the use of broad-spectrum antibiotics to the treatment of verified bacterial infection can best prevent this life-threatening complication.

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